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**Docket No. 200427US0 CONT**

**IN THE UNITED STATES PATENT & TRADEMARK OFFICE**



IN RE APPLICATION OF :

Claudio CAVAZZA : EXAMINER: G. KISHORE

SERIAL NO.: 09/777,874 :

FILED: FEBRUARY 7, 2001 : GROUP ART UNIT: 1615

FOR: PHARMACEUTICAL COMPOSITON COMPRISING L-CARNITINE OR ALKANOYL L-CARNITINE, FOR THE PREVENTION AND TREATMENT OF DISEASES BROUGHT ABOUT BY LIPID METABOLISM DISORDERS.

DECLARATION UNDER 37 C.F.R. §1.132

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Now comes FRANCO GAETANI who deposes and states:

1. That I am a graduate of "La Sapienza" University in Rome (Italy) and received my Chemistry degree in the year 1973.

2. That I have been employed by Sigma-Tau Group for 24 years in the field of Research & Development:
from 1977 to 1989 as assistant to the Research Director;
from 1989 to 1998 as person in charge of the Research Laboratories organization; since 1998 I have been the Research & Development Director of Sigma-Tau HealthScience.

3. That the statistical data presented below were obtained by me or under my direct supervision and control.

4. The statistical significance of the differences between groups receiving the combination of calcium hydroxycitrate (HCA) and acetyl L-carnitine and groups receiving only calcium hydroxycitrate (HCA), only acetyl L-carnitine, or no treatment (control) were determined using the Student's T test. A "p value" of less than .05($p<05$) is conventionally accepted as showing a significant difference between groups. The "p values" of groups

receiving the combination of HCA and acetyl-L-carnitine ("***") compared to various control groups are shown in Tables 2, 4 and 5 below. These results demonstrate that administration of HCA and acetyl-L-carnitine produces significant decreases in body weight (Table 1), significant reductions in triglycerides (Table 4) and significant reductions in cholesterol (Table 5) compared to the administration of HCA alone or acetyl-L-carnitine alone.

**TABLE 2**

**BODY WEIGHT INCREASE AFTER 15 DAY-TREATMENT**

| | Final body weight increase (g) | p-value |
|---|---|---|
| **Controls** | **62.8 ± 3.5** | **p<.001** |
| **Calcium hydroxycitrate (g 1/100 g diet)** | **46.6 ± 4.1** | **p<.001** |
| Calcium hydroxycitrate (g 2/100 g diet) | 38.9 ± 3.8 | |
| L-carnitine (g 2/100 g diet) | 66.2 ± 4.9 | |
| L-carnitine (g 4/100 g diet) | 64.5 ± 5.1 | |
| **Acetyl L-carnitine (g 2/100 g diet)** | **60.4 ± 7.1** | **p<.002** |
| Acetyl L-carnitine (g 4/100 g diet) | 60.1 ± 6.1 | |
| Propionyl L-carnitine (g 2/100 g diet) | 62.4 ± 3.9 | |
| Propionyl L-carnitine (g 4/100 g diet) | 58.7 ± 3.7 | |
| Garcinia cambogia (g 4/100 g diet) | 51.4 ± 3.3 | |
| Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet) | 28.7 ± 4.4 | |
| **Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)** | **31.6 ± 3.9** | *** |
| Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet) | 24.4 ± 2.8 | |
| L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 38.6 ± 3.1 | |
| Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 36.8 ± 4.4 | |
| Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 34.8 ± 6.5 | |

**TABLE 4**

**TEST ON EXPERIMENTALLY-INDUCED HYPERTRIGYCERIDAEMIA**

**(mg/100 ml)**

| | | |
|---|---|---|
| **Controls** | **195.8 ± 9.8** | **p<.001** |
| **Calcium hydroxycitrate (g 0.5/Kg)** | **170.6 ± 8.5** | **p<.001** |
| Calcium hydroxycitrate (g 1/Kg) | 145.5 ± 8.5 | |
| L-carnitine (g 0.5/Kg) | 190.4 ± 9.6 | |
| L-carnitine (g 1/Kg) | 190.8 ± 8.6 | |
| **Acetyl L-carnitine (g 0.5/Kg)** | **191.2 ± 9.1** | **p<.001** |
| Acetyl L-carnitine (g 1/Kg) | 188.4 ± 5.5 | |
| Propionyl L-carnitine (g 0,5/Kg) | 184.2 ± 6.8 | |
| Propionyl L-carnitine (g 1/Kg) | 180.4 ± 7,9 | |
| Garcinia cambogia (g 0.5/Kg) | 170.6 ± 5.4 | |
| Calcium hydroxycitrate (g 0.5/Kg) + L-carnitine (g 0.5/Kg) | 125.8 ± 9.1 | |
| **Calcium hydroxycitrate (g 0.5/Kg) + Acetyl L-carnitine (g 0.5/Kg)** | **120.4 ± 8.8** | *** |
| Calcium hydroxycitrate (g 0.5/Kg) + Propionyl L-carnitine (g 0.5/Kg) | 108 ± 9.4 | |
| L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0,5/Kg) | 145.4 ± 8.6 | |
| Acetyl L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0.5/Kg) | 140.4 ± 7.4 | |
| Propionyl L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0.5/Kg) | 125 ± 8.5 | |

**TABLE 5**

**TESTS ON EXPERIMENTALLY-INDUCED HYPERCHOLESTEROLEMIA**

**(TOTAL CHOLESTEROL mg/dl)**

| | | |
|---|---|---|
| Controls | 92.5 ± 4.4 | |
| **Hypercholesterolemic controls** | **270.5 ± 10.4** | **p<.001** |
| **Calcium hydroxycitrate (g 1/100 g diet)** | **196.6 ± 9.6** | **p<.001** |
| Calcium hydroxycitrate (g 2/100 g diet) | 180.5 ± 8.1 | |
| L-carnitine (g 2/100 g diet) | 270.4 ± 5.1 | |
| L-carnitine (g 4/100 g diet) | 260.6 ± 4.4 | |
| **Acetyl L-carnitine (g 2/100 g diet)** | **266.7 ± 7.7** | **p<.001** |
| Acetyl L-carnitine (g 4/100 g diet) | 255.4 ± 9.4 | |
| Propionyl L-carnitine (g 2/100 g diet) | 250.6 ± 10.1 | |
| Propionyl L-carnitine (g 4/100 g diet) | 235.3 ± 9.6 | |
| Garcinia cambogia (g 4/100 g diet) | 250.7 ± 4.7 | |
| Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet) | 155.8 ± 8.8 | |
| **Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)** | **150.5 ± 7.1** | *** |
| Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet) | 110.6 ± 6.6 | |
| L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 179.6 ± 9.6 | |
| Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 165.9 ± 8.9 | |
| Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet) | 55.5 ± 6.8 | |

8. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

9. Further deponent saith not.

Dec 14/2001
Date

Signature

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